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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,417	12/19/2005	Dan Peters	2815-0338PUS1	6546

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EXAMINER

RAHMANI, NILOOFAR

ART UNIT	PAPER NUMBER
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1625

NOTIFICATION DATE	DELIVERY MODE
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06/11/2007

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/561,417

Applicant(s)

PETERS ET AL.

Examiner

Niloofer Rahmani

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-14 are pending in the instant application and claim 15 is cancelled.

Priority

2. This application is filed on 12/19/2005, which is a 371 of PCT/EP04/51167, filed on 06/18/2004, which claims benefit of 60/482,566, filed on 06/26/2003, and claims benefit of 60/509,808, filed on 10/10/2003, and claims benefit of 60/544,210, filed on 02/13/2004, which claims priority of DENMARK PA 2003 00939, filed on 06/24/2003, and claims priority of DENMARK PA 2003 01487, filed on 10/09/2003, and claims priority of DENMARK PA 2004 00228, filed on 02/13/2004.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-14 are rejected because the term "alleviation" is confusing.

What is alleviation means? Correction is required.

4. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

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The nature of the invention: The instant invention is drawn to method for treating a disease or a disorder or condition or mood disorder using a compound of claim 1.

The state of the prior art: " Treatment of PC12 cells with MPP⁺ for 48 h induced apoptotic death as determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and flow cytometry, the activation of caspase-3 measured by the caspase-3 activity assay kit, the reduction in mitochondrial membrane potential with laser scanning confocal microscopy and the increase in the extracellular hydrogen peroxide level. Simultaneous treatment with verbascoside markedly attenuated MPP⁺ induced apoptotic death, increased extracellular hydrogen peroxide level, the activation of caspase-3 and the collapse of mitochondrial membrane potential. These results strongly indicated that verbascoside may provide a useful therapeutic strategy for the treatment of oxidative stress-induced neurodegenerative disease such as Parkinson's disease." (Sheng et al., European journal of pharmacology, 2002, Vol. 451, pages 119-124)

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that

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in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be useful for treating or preventing disorder diseases is efficacious.

Amount of guidance/working examples: Applicant provides no guidance for how compounds of formula (I) could treat or prevent any and all known diseases.

There are no working examples in the instant application showing that the instant compounds can treat or prevent disorder diseases. nor are there any examples of the disease being either treated or prevented by the compounds of formula (I).

The breadth of the claims: The breadth of claims is drawn to method for treating a disease or a disorder or condition or mood disorder using a compound of claim 1.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating or preventing disorder diseases is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

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Taking all of the above into consideration, it is not seen where the instant claims 12-14, for treating or preventing disorder diseases is efficacious, have been enabled by the instant specification.

5. Claims 12-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases

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requires identifying those patients who will acquire the disease before occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 9, page 15 to line 35, page 15 lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted with diseases before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of disorder diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent disorders generally. That is, the skill is so low that no compound effective generally against disorders has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies

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inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prevention".

6. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

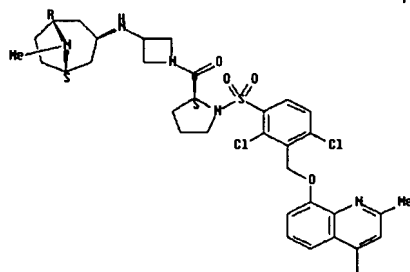
Claims 1,3-4,6, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Ananthan et al., Bioorganic & Medicinal chemistry letters, 2002, Vol. 12, pages 2225-2228. Ananthan et al. disclosed the instant claimed compound on page 2227, Table 1., compound 4a. Therefore, the instant claim is anticipated by Ananthan et al.

7. Claims 1,3,6,and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Yasuhiro et al. EP 1213289. Yasuhiro et al. disclosed the instant claimed compound, which are from the STN search

CN 3-Azetidinamine, 1-[[[(2S)-1-[[2,4-dichloro-3-[[2,4-dimethyl-8-quinolinyl)oxy]methyl]phenyl]sulfonyl]-2-pyrrolidinyl]carbonyl]-N-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-

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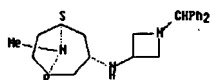
PAGE 1-A



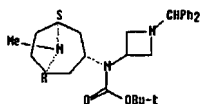
PAGE 2-A

Me

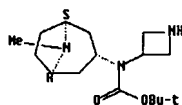
CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[1-(diphenylmethyl)-3-azetidinyl]-8-methyl-, (3-exo)



CN Carbamic acid, [1-(diphenylmethyl)-3-azetidinyl][(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester



CN Carbamic acid, 3-azetidinyl[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester

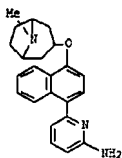


Therefore, the instant claim is anticipated by Yasuhiro et al.

8. Claims 1,3-4, 6-7, and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Saltarelli et al., WO 2000071107. Saltarelli et al. disclosed the instant claimed compound, which are from the STN search

RN 310431-78-8

CN 2-Pyridinamine, 6-[4-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]-1-naphthalenyl]

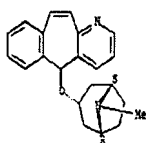


Therefore, the instant claim is anticipated by Saltarelli et al.

9. Claims 1,3-4, 6-7, and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Bakken et al., Journal of medicinal chemistry, 2000, Vol. 43, pages 4534-4541. Bakken et al. disclosed the instant claimed compound, which are from the STN search

RN 19410-02-7

CN 5H-Benzo[4,5]cyclohepta[1,2-b]pyridine, 5-[[[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]oxy]

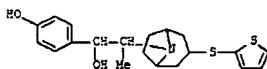


. Therefore, the instant claim is anticipated by Bakken et al.

10. Claims 1,3,5, 6,8, and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Chenard et al., US 5710168. Chenard et al. disclosed the instant claimed compound, which are from the STN search

RN 134138-54-8

CN 8-Azabicyclo[3.2.1]octane-8-ethanol, a-(4-hydroxyphenyl)-b-methyl-3-(2-thienylthio)-, stereoisomer

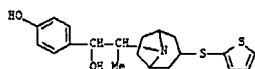


RN 134234-08-5

CN 8-Azabicyclo[3.2.1]octane-8-ethanol, a-(4-hydroxyphenyl)-b-

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methyl-3-(2-thienylthio)-, stereoisomer

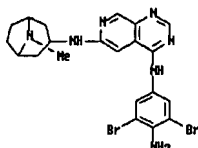


Therefore, the instant claim is anticipated by Chenard et al.

11. Claims 1,3, 6, and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Himmelsbach et al., WO 9732881. Himmelsbach et al. disclosed the instant claimed compound, which are from the STN search

RN 196796-64-2

CN Pyrido[3,4-d]pyrimidine-4,6-diamine, N4-(4-amino-3,5-dibromophenyl)-N6-(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)



Therefore, the instant claim is anticipated by Himmelsbach et al.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas Mckenzie, can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair->

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NILOOFAR RAHMANI

D.MARGARET SEAMAN

05/22 /2007

PRIMARY EXAMINER

Nr

GROUP 1625

A handwritten signature in black ink, appearing to read "D. Margaret Seaman", is written over the printed name and title.